REMARKS

Status of the Claims

Claims 1-39 are pending and claims 18, 20-24, and 26-29 are under consideration in this application, claims 1-17, 19, 25, and 30-39 having been withdrawn for allegedly being drawn to separate inventions. After entry of the amendments made herein, claims 1-21 and 23-39 will be pending and claims 18, 20-21, 23-24, and 26-29 will be under consideration, claim 22 having been cancelled without prejudice to its being presented in a separate application.

Sequence Listing

As requested on page 11, lines 5-8, of the Office Action, a Sequence Listing for the instant application is enclosed herewith. Applicants hereby submit that the enclosures fulfill the requirements under 37 C.F.R. §1.821-1.825. Applicants enclose herewith a Sequence Listing in computer-readable form as required by 37 CFR §1.824. In addition, Applicants submit a paper copy of the Sequence Listing as required under 37 CFR §1.823(a)(1) and a statement under 37 CFR §1.821(f). Applicants respectfully request entry of the paper copy and computer-readable copy of the Sequence Listing filed herewith for the instant application. No new matter has been added. In addition the specification is amended to conform it to the Sequence Listing. No new matter is added by the amendments.

Double Patenting Rejection

Claims 18, 20-23, 26, 27, and 29 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-11 of U.S. Patent No. 6,001,329 (the'329 patent). Applicants respectfully traverse this rejection.

Applicants understand the Examiner's position to be that the claims of the '329 patent render obvious the claims presently under consideration in the instant application. Applicants disagree with this position.

The claims of the '329 patent specify: (a) a composition containing a recombinant fusion toxin composed of a toxin, a targeting moiety, a radionuclide; and (b) methods of killing and

treating a tumor cell. The targeting moiety of the '329 patent's fusion toxin is one "which binds to a receptor overexpressed by tumor cells" (see claim 1 of the '329 patent). In the present application, the targeting moiety (domain) is "a sFv antibody fragment that binds to a target cell molecule on a target cell in [a] subject" (see instant claim 18).

Applicants respectfully submit that one of ordinary skill in the art reading the specification of the '329 patent would not understand: (i) the targeting moieties (i.e., those that bind to a "receptor overexpressed by tumor cells") of the '329 patent's fusion toxins to include any form of antibody, let alone sFv fragments; or (b) sFv fragments to be obvious variants of targeting moieties covered by the claims.

The specification of the '329 patent is replete with text in which the two categories of targeting moieties are distinguished. Thus, for example, it is stated that "[t]his effect can best be realized with intranuclear localization of the radionuclide, which does not generally occur with radiolabeled MoAbs, but may occur with certain membrane receptor-radioligand interactions." (sentence spanning columns 2 and 3). The first paragraph of the "Summary of the Invention" section begins: "The present invention describes the synthesis of a new class of compounds known as radiolabeled fusion toxins (RFT), in which both toxin and radionuclide tags are contained on the same growth factor (murine granulocyte macrophage colony stimulating factor (MGM-CSF) or murine interleukin-4 (mIL-4)" (column 8, lines 21-27). Moreover, the first paragraph of the "Detailed Description of the Invention" section that provides examples of all three components of the '329 patent's fusion toxin states that "[r]epresentative examples of a targeting moiety that binds to receptors overexpressed by tumor cells is selected from the group consisting of the interleukin-4, interleukin-2, epidermal growth factor and the granulocyte macrophage colony stimulating factor." (column 13, lines 28-32).

In view of the fact that the Background section of '329 patent that discusses the prior art specifically mentions as targeting moieties antibody and antibody fragments (including sFv) as well as cytokines and growth factors, it is telling that in the descriptions of the invention of the '329 patent itself (e.g., the text from the Summary of the Invention and the Detailed Description of the Invention sections quoted above), there is no mention of using antibodies or antibody

fragments as targeting moieties. In light of this discrepancy in the teaching of the '329 patent in regard, on one hand, to the prior art and, on the other hand, the invention of the '329 patent, one of ordinary skill in the art would conclude that the inventors of the '329 patent intended not to include antibodies and antibody fragments (such as sFv fragments) in the class of targeting moieties used in the fusion toxins specified by its claims.

In view of the above considerations, Applicants respectfully request that rejections under the judicially created doctrine of obviousness-type double patenting be withdrawn.

35 U.S.C. §112, first paragraph, rejection

Claims 18, 20-24, and 26-29 stand rejected on the grounds that the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with claims.

From the text on page 4, line 10, to page 6, line 13, of the Office Action, Applicants understand the Examiner's position to be that, while the specification is enabling for methods in which the pathogenic cell disease is cancer, it is not enabling for methods applied to pathogenic cell diseases in general. Applicants do not agree with this position. However, in order to expedite prosecution of the instant application, Applicants have amended claim 1 by replacing "pathogenic cell disease" with cancer and by substituting target cell with "cancer cell". These amendments are supported by the specification (e.g., at page 9 lines 2-7; page 13, lines 24-25; and page 16, lines 3-31) and add no new matter. In addition, claim 22 is cancelled and the dependency of claim 23 is been changed from claim 22 to claim 18.

With respect to the Examiner's concerns regarding the types of methods the claims cover, Applicants respectfully submit that the steps of the method specified by claim 18 are quite clear and unequivocal and that the claim would cover any method in which such steps were performed. For example, one of skill in the art would appreciate that the method could be performed for the purpose of studying the biodistribution or pharmacokinetics of the radiolabeled immunotoxin (see, e.g., the biodistribution experiment described in Example 2 of the instant specification), in addition to killing a cell or imaging.

In light of the above amendments, Applicants respectfully request that the rejection under 35 U.S.C. §112. first paragraph, be withdrawn.

35 U.S.C. §112, second paragraph, rejection

Claims 18, 20-24, and 26-29 stand rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

With respect to the rejection on page 6, lines 21-22, of the Office Action, the comments in the section above relating to the types of methods covered by the instant claims are pertinent.

Applicants submit that rejection on page 7, lines 1-2, of the Office Action, is moot in view of the above-described amendments to claim 18.

In light of the above considerations, Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph, be withdrawn.

35 U.S.C. §102(b) rejection

Claims 18, 20, 21, 26, and 27 stand rejected as allegedly being anticipated by Vallera et al. Applicants respectfully traverse the rejection.

Applicants understand the Examiner's position to be that Vallera et al., in disclosing the administration of the ^{125}I-labeled DT_{390}-anti-CD3sFv immunotoxin to mice, anticipates the instant claims. Applicants disagree with this position. As is clear from the reference, the ^{125}I-labeled DT_{390}-anti-CD3sFv immunotoxin was injected only into normal mice for pharmacokinetic studies (e.g., page 2345, column 1, paragraphs 3 and 4; and page 2348, column 2, paragraph 1). Thus, the disclosure of Vallera et al. with respect to the radiolabeled immunotoxin lacks crucial aspects of both steps of the method of the present invention, i.e., "identifying a subject suspected of having cancer" and "administering to the subject a radiolabeled immunotoxin."

In light of the above considerations, Applicants respectfully request that the rejection under 35 U.S.C. §102(b) be withdrawn.

35 U.S.C. §103(a) rejections

(a) Claims 18, 20-23, and 26-29 stand rejected as allegedly being unpatentable over Vallera et al. in view of U.S. Patent No. 5,332, 567 (the '567 patent). Applicants respectfully traverse this rejection.

The teaching of Vallera et al. is described above. The '567 patent describes treatment and imaging in infectious diseases using antibody conjugates. The '567 patent., makes no mention of cancer, let alone identifying a subject suspected of having a cancer. Thus, the '567 patent fails to remedy this defect in Vallera et al. Hence, neither reference, taken alone or in combination with the other, renders the invention of the instant claims obvious.

(b) Claims 18, 20-23, and 26-29 stand rejected as allegedly being unpatentable over Thompson et al. in view of the '567 patent. Applicants respectfully traverse this rejection.

From the comments on page 10, line 15, to page 11, line 3, Applicants understand the Examiner's position to be that Thompson et al. (in disclosing an immunotoxin containing an anti-CD3 sFv and DT390) in combination with the '567 patent (in disclosing methods of detecting, imaging, and treating infection and labeling of immunoconjugates with radioisotopes) render the instant invention obvious.

Thompson et al. does not disclose, or even suggest, identifying a subject suspected of having cancer and administering a sFv-containing immunotoxin (radiolabeled or unlabeled) to the subject. The reference in Thompson et al. to the *in vitro* experiments described in the paper "mimic[king] the *in vivo* situation" (page 28040, column 1, paragraph 2) certainly does not amount to a disclosure or suggestion of administering an immunotoxin to a subject suspected of having cancer. Moreover, the immunotoxin described in Thompson et al. was radiolabeled for use only in an *in vitro* endocytosis assay, i.e., not for administration to a subject suspected of having cancer (e.g., page 28038, paragraph spanning columns 1 and 2, and column 2, paragraph 3).

The '567 patent makes no mention of sFv-containing immunoconjugates, let alone administering a radiolabeled sFv-containing immunoconjugate to a subject. More importantly, the radiolabeled immunoconjugates that the '567 patent does describe are used for the purposes of detecting, imaging, and treating microbial infections only, i.e., not for administering to subjects suspected of having cancer. Hence, the '567 patent does not cure the Thompson et al. reference's failure to disclose identifying a subject suspected of having cancer and administering a radiolabeled sFv-containing immunotoxin to the subject.

In conclusion, neither singly nor in combination do Thompson et al. and the '567 patent render the invention of the instant claims obvious.

In light of the above considerations, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103(a).

CONCLUSION

In summary, for the reasons set forth above, Applicants maintain that the pending claims patentably define the invention. Applicants request that the Examiner reconsider the rejections as set forth in the Office Action, and permit the pending claims to pass to allowance.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' undersigned representative can be reached at the telephone number listed below.

Applicants submit herewith a request for an extension of time and a check in payment of the extension in time. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 09531-023001.

Respectfully submitted,

Date: 10/20/03

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